Thieme

Sedentary Behavior and Arterial Stiffness in Adults with and without Metabolic Syndrome

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ABSTRACT

This study aimed to investigate whether sedentary time (Sed) and physical activity (PA) are associated with arterial stiffness in individuals with and without metabolic syndrome (MetS). This cross-sectional study comprised 197 individuals (47 ± 13 years; 58 % female) from a primary health care centre. Arterial stiffness was assessed using carotid-femoral pulse wave velocity (cfPWV). Metabolic syndrome was determined as clustering of at least 3 out of 5 risk factors (central obesity, hypertension, impaired glucose, triglycerides and high-density lipoprotein cholesterol). Daily PA was objectively assessed and classified in Sed, light and moderate-to-vigorous PA. Physical activity was used as a continuous variable for multiple regression analysis. For mean comparisons of cfPWV between subjects with and without MetS, a binary split at the median of Sed and PA was used. Sedentary time was associated with cfPWV ($\beta = 0.11$; $p = 0.01$) explaining 1.3 % of its variance; independently of age ($\beta = 0.49$; $p < 0.001$), systolic blood pressure ($\beta = 0.27$; $p < 0.001$) and fasting glucose ($\beta = 0.19$; $p < 0.001$). Participants with MetS and more Sed had higher cfPWV than those with MetS and less Sed (9.9 ± 1.0 vs. 8.9 ± 1.0 m/s; $p < 0.05$). Sedentary time is associated with cfPWV independently of age and metabolic risk factors. A higher Sed in MetS individuals lead to a worse arterial stiffness profile.

Introduction

Metabolic syndrome (MetS) involves a cluster of interrelated risk factors, including raised blood pressure, dyslipidemia, raised glucose and central obesity [2], which double the risk of cardiovascular events [2, 14]. Given its growing prevalence worldwide, coupled with an obesity pandemic and increase in sedentary lifestyles, MetS has become a major public health problem [2].

Evidence has shown that the odds of developing MetS increase with sedentary behavior (Sed) [11, 12], independently of individuals meeting international guidelines for moderate-to-vigorous physical activity (MVPA) [6]. Improved MVPA concomitant with less Sed is an important goal for the primary prevention of MetS [2].

MetS is also associated with a chronic inflammatory and prothrombotic state [2], which prompts vascular arterial wall remodeling characterized by incremental arterial stiffness (AS) [23, 25]. By extension, given its association with fatal and nonfatal cardiovascular events, AS is an important risk factor for cardiovascular disease (CVD) [28].

Although AS is largely determined by age and metabolic risk factors, the impact of lifestyle upon the condition is not negligible [19]. However, to the best of our knowledge, the independent association between physical activity (PA) and AS, is poorly established, as is whether higher levels of MVPA and reduced Sed mitigate the deleterious effects of age and MetS upon AS.

In response, in this study we investigated the relationship among AS, objective measures of daily PA intensity and Sed in individuals either with or without MetS.

Materials and Methods

Study design

This cross-sectional study was conducted in a primary health care center (Porto, Portugal). Inclusion criterion was age ≥ 18 and ≤ 65 years old. Exclusion criteria were established CVD or cognitive dis-

orders, neurological and orthopedic impairments, arrhythmias, severe hypertension [systolic blood pressure (SBP) > 180 mmHg or diastolic blood pressure (DBP) > 100 mmHg], acute coronary syndromes and peripheral arterial disease, thyroid disorders, severe pulmonary and renal disorders, or infectious and chronic immunological diseases.

Participants

Participants were recruited from database including 8 000 registered individuals. An age filter was applied to the database, leaving 4 600 potential participants. From those, 1 200 were random sampled in 6 unique sets of 200 numbers. This study enrolled the general population, because participants were randomly selected from the registries of the primary health care centre. In Portugal access to National Health Service is universal, and everyone is registered, even those who do not access healthcare services [9]. The study was approved by the Ethics Committee of the North Regional Health Authority (I.P. 25/2010) and met the ethical standards of the International Journal of Sports Medicine [15].

Data collection

Participants were invited through phone calls and those who accepted went twice to the health care centre. Participants were instructed to refrain from strenuous exercise and to avoid consuming caffeine-containing products or alcohol for at least 24 h before evaluation. During the first appointment, eligibility criteria, data on sociodemographics, pre-existing clinical conditions and medications were verified. In this appointment, anthropometrics, blood pressure and AS were taken and each participant was given an accelerometer. After 7 days, participants returned for the second appointment to return the accelerometers and to collect blood samples.

Anthropometry and clinical variables

Height was assessed with a standard wall-mounted stadiometer and weight using a scale (Tanita, Inner Scan BC-522, Japan). Body mass index (BMI) was calculated as the ratio of weight to squared height. Waist circumference was measured at the midpoint between the lowest rib and iliac crest. MetS was defined as the clustering of at least 3 out of 5 conditions: central obesity (waist circumference ≥ 102 cm in men and ≥ 88 cm in women); triglycerides ≥ 150 mg/dL or drug treatment for elevated triglycerides; high density lipoprotein (HDL) cholesterol < 40 mg/dL in men and < 50 mg/dL in women or drug treatment for reduced HDL-cholesterol; SBP ≥ 130 and/or DBP ≥ 85 mmHg or presence of antihypertensive medication; and, elevated fasting glucose (≥ 100 mg/dL) or drug treatment for elevated glucose [2].

Blood pressure and AS measurements

A single trained researcher performed blood pressure and AS measurements after 20 min resting in supine position. Blood pressure was assessed (Colin, BP 8 800; Critikron, Inc., USA) in the left arm and SBP and DBP were computed as the average of 3 readings. Additional readings were performed when differences between readings exceeded 5 mmHg. SBP and DBP were used to calculate pulse pressure and mean blood pressure [7]. AS was measured as carotid-femoral pulse wave velocity (cfPWV) using the SphygmoCor device (AtCor Medical, Australia) according to international guidelines [7]. Two valid measures were perfomed and the average was used for analysis. AS assessment was made at rest in a quiet, semi-dark room with an average temperature of 21 °C.

Physical activity

Daily PA was assessed using accelerometers (Actigraph GT1M, Actigraph LLC, Pensacola, FL) over the right hip, for 7 consecutive days, during the waking hours, except while bathing and water-based activities [10]. ActiLife software (Actigraph, Florida, USA, version 6.9) was used to reduce raw activity data into daily PA. The accelerometer measures the intensity of movement, which was averaged for 1-min sampling intervals (counts/min). For data analysis, non-wear periods were defined as ≥ 10 consecutive 1-min sampling intervals with "zero" counts. To be considered as valid data, individuals must have had a minimum of 4 days recorded with at least 8 wear-time hours per day. The average minutes/day spent at different categories of PA intensity was determined according to cut points that relate PA to counts/min: sedentary (Sed) time (≤ 99 counts/min), light PA (LPA) (100–2 019 counts/min) and MVPA (≥ 2 020 counts/min) [26].

Blood sampling

Twelve hours fasting blood samples were collected by venipuncture of the antecubital vein into serum separator and EDTA coated tubes. The following parameters were assessed: glycated hemoglobin (HbA1c), serum glucose, total cholesterol, HDL-cholesterol, triglycerides, high-sensitivity C-reactive protein (hs- CRP) and plasma insulin. Low-density lipoprotein (LDL) was calculated using the Friedewald equation. A high sensitive Milliplex map kit (Millipore, Germany), with the Luminex 200™ analyzer (Luminex Corporation, USA) were used to assess the plasma Interleukin-6 (IL-6), Tumor Necrosis Factor alpha (TNF-a) and leptin. Adiponectin plasma levels were determined using a commercial enzyme-linked immunosorbent assay (Mercodia AB, Sweden). The ratio leptin-to-adiponectin was calculated dividing leptin by adiponectin [1]. Assays were assessed in duplicated.

Statistical methods

Not normally distributed variables were transformed into a natural logarithm (cfPWV) or ranked (LPA and MVPA) for analysis and then transformed back to the original scale for the purpose of clarity. Data are expressed as mean ± standard deviation.

Pearson's correlation was used to analyze the relationship between cfPWV and PA for the total sample. Multivariate linear regression with stepwise selection of variables was performed to determine the relationship between cfPWV, risk factors and PA. Variables were organized in clusters in order to sort out the contribution of redundant variables (i. e., morphometric, lipid, inflammatory, diabetes and hypertension) [8]. Within each cluster, variables were included in a competitive manner in multivariate models. The variable with the highest univariate significant level with cfPWV was kept. Variables retained from clusters were tested with age. Those that sustained the significant level were included in the first model. The second model, encompassed variables retained from the first model plus PA variables with bivariate significant association with cfPWV.

The sample was classified according to the presence or absence of MetS and then MetS and non-MetS groups were divided by the median of PA levels and Sed. Comparisons between groups were performed using independent t-test, chi-square and ANCOVA, with Bonferroni post hoc test. For these analyses, mean and standard error were adjusted for age. Statistical analysis was performed using the IBM SPSS 20 software (SPSS, USA). Power analysis was calculated post hoc and it was higher than 0.8. P-values < 0.05 were considered significant.

Results

From the 1 200 individuals randomly sampled, 318 did not answer, 244 declined to participate, 348 had exclusion criteria and 33 missed the first appointment. A total of 257 individuals attended to the study and 197 had valid data for AS and PA, being considered the final sample size.

Sample characteristics are presented in ▶ **Table 1**. Regarding PA, mean wear time was 13.3 ± 1.5 h/day, ranging from 8.7 to 17.5 h/day.

Comparisons between participants with and without MetS showed that those with MetS tended to be older, exhibit significantly worse indexes for MetS risk factors, had greater inflammatory biomarkers and cfPWV (▶ **Table 1** , **2**).

Considering the total sample, cfPWV was positively associated with Sed (r = 0.14; p = 0.03), and negatively associated with MVPA (r = − 0.20; p = 0.005). The correlation between cfPWV and light PA was not significant (r = − 0.05, p = 0.48).

▶ **Table 3** shows 2 multivariate models for the natural logarithm of cfPWV. Since not all clusters were significant predictors for cfPWV, some clusters have no variables in the first model. In the second model, Sed became an independent predictor of cfPWV (β = 0.11; p = 0.01) that explained 1.3 % of its variance. However, MVPA was not an independent predictor of cfPWV (p > 0.05).

▶ **Fig. 1** presents the results for ANCOVA. Participants with MetS who spent more Sed showed significantly greater cfPWV than not only those with MetS and less Sed, but also all individuals in both non-MetS groups regardless of Sed (▶ **Fig. 1a**). However, that pattern did not emerge in the distinction between light PA (▶ **Fig. 1b**) and MVPA (▶ **Fig. 1c**), since individuals with MetS who engaged greater PA had the same mean cfPWV value as those who engaged less PA.

▶ **Table 1** Sample characteristics and between groups comparison.

	Overall (n = 197)	No MetS (n = 116)	With MetS (n = 81)
Age, years	47 ± 13	42 ± 12	54 ± 10 * *
Female, n (%)	114 (58)	71 (61)	43 (53)
Body mass index, kg/m^2	26.8 ± 4.3	25.2 ± 3.9	29.0 ± 3.9 * *
Waist circumference, cm	92 ± 12	88 ± 11	99 ± 10 * *
Risk factors and medications			
Hypercholesterolemia, %	71	60	88 * *
Hypertension, %	43	16	82 * *
Type II Diabetes, %	9	0	22 * *
Obesity, %	20	9	37 * *
Current smoker, %	29	35	22 *
Antihypertensive, %	33	14	61 * *
Lipid-lowering, %	22	1	53 * *
Oral anti-diabetic, %	8	0	20 * *
Blood pressure, heart rate and arterial stiffness			
Brachial systolic blood pressure, mm Hg	127 ± 16	120 ± 13	137 ± 15 * *
Brachial diastolic blood pressure, mm Hg	75 ± 11	71 ± 10	80 ± 10 * *
Mean blood pressure, mm Hg	94 ± 13	89 ± 12	102 ± 12 * *
Brachial pulse pressure, mm Hg	52 ± 10	49 ± 8	57 ± 11 * *
Aortic pulse pressure, mm Hg	41 ± 10	38 ± 9	47 ± 10 * *
Resting heart rate, bpm	64 ± 9	63 ± 10	64 ± 9
cfPWV, m/s	9.1 ± 1.9	8.3 ± 1.5	10.2 ± 1.9 * *
Physical activity			
Mean wear time, min/day	798 ± 90	792 ± 96	804 ± 90
Sedentary time, min/day	460 ± 93	455 ± 93	469 ± 92
Light PA, min/day	301 ± 99	299 ± 100	305 ± 99
Moderate-to-vigorous PA, min/day	36 ± 26	39 ± 27	32 ± 24 *

Hypercholesterolemia = total cholesterol > 190 mg/dL; and/or low-density lipoprotein > 115 mg/dL; and/or, high-density lipoprotein: men < 40 mg/dL, women < 46 mg/dL; and/or presence of lipid lowering medication. Obesity = body mass index ≥ 30 kg/m^2. cfPWV: carotid-femoral pulse wave velocity; PA: physical activity

* p < 0.05; * * p < 0.001

▶ **Table 2** Overall and between groups comparisons for lipid, metabolic, inflammatory and hormonal characteristics.

	Overall	No MetS	With MetS
Lipid profile			
Triglycerides, mg/dL	111.4 ± 55.8	93.2 ± 37.6	138.7 ± 66.9 * * *
HDL- Cholesterol, mg/dL	56.9 ± 15.2	59.4 ± 15.3	50.5 ± 13.4 * * *
LDL-Cholesterol, mg/dL	118.9 ± 35.8	115.7 ± 35.1	123.9 ± 36.6
Total Cholesterol, mg/dL	197.1 ± 38.6	193.6 ± 37.1	202.7 ± 40.4
Metabolic profile			
Fasting glucose, mg/dL	96.1 ± 29.5	86.1 ± 10.4	111.2 ± 40.6 * * *
Insulin, µlU/mL	10.3 ± 7.0	8.5 ± 5.3	13.0 ± 8.4 * * *
Glycated hemoglobin, %	5.5 ± 0.7	5.2 ± 0.2	5.8 ± 0.9 * * *
Inflammatory biomarkers			
hs C-reactive protein, mg/dL	0.3 ± 0.6	0.2 ± 0.4	0.4 ± 0.8 *
Interleukin-6, pg/mL	1.8 ± 1.5	1.6 ± 1.4	2.2 ± 1.6 * *
TNF α, pg/mL	3.3 ± 1.4	3.0 ± 1.2	3.7 ± 1.6 * *
Adipocyte-specific proteins			
Leptin, mg/mL	13.6 ± 12.0	13.2 ± 13.1	14.0 ± 10.4
Adiponectin, mg/mL	10.7 ± 5.2	11.3 ± 5.5	10.0 ± 4.6 *
Leptin-to-Adiponectin ratio	1.3 ± 1.3	1.2 ± 1.1	1.6 ± 1.6 * *

HDL: High-density lipoprotein cholesterol; LDL: low-density lipoprotein; TNFα: tumor necrosis factor alpha. * p < 0.05; * * p < 0.01; * * * p < 0.001

▶ **Table 3** Multivariate relationship between natural logarithm of carotid-femoral pulse wave velocity and independent variables.

Parameters	R^2 increment %	Beta	p
Model 1 (R^2: 0.56)			
Age, years	44.6	0.49	< 0.001
Systolic blood pressure, mm Hg	8.2	0.27	< 0.001
Fasting glucose, mg/dL	3.7	0.20	< 0.001
Model 2 (R^2: 0.58)			
Age, years	45.5	0.49	< 0.001
Systolic blood pressure, mmHg	7.7	0.27	< 0.001
Fasting glucose, mg/dL	3.5	0.19	< 0.001
Sedentary time, min/day	1.3	0.11	0.01

The dependent variable (cfPWV) is in natural logarithm. Beta: standardized coefficients

Discussion

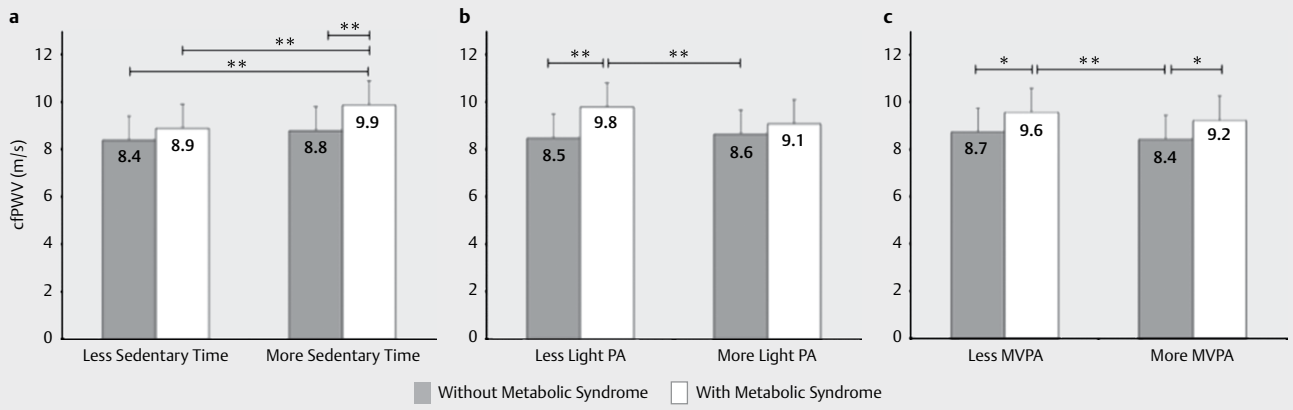
The findings of the study are twofold: Sed is independently associated with cfPWV in participants with or without MetS, and individuals with MetS and more Sed display a significantly greater cfPWV than those with MetS and less Sed. To the best of our knowledge, our study is the first to investigate the interaction of daily PA and MetS on cfPWV at the same time.

Our multivariate analysis explained nearly half (R^2 = 58 %) of all variation in cfPWV, 1.3 % of which was explained by Sed. As clinical values indicate, for individuals of the same age with similar SBP and fasting glucose, Sed augments cfPWV.

Despite the abovementioned, the combination of MetS with more Sed precipitated greater cfPWV close to 10 m/s, which indicates a risk of a cardiovascular event [20]. In our analysis, we removed the effect of age and controlled for it with MVPA. Since both MetS and non-MetS groups demonstrated sufficient MVPA (i. e., > 30 min/day) the overall results suggest that sufficient MVPA does not negate the effects of Sed. Indeed, earlier studies examined the association between AS and Sed in apparently healthy populations [16, 27], and despite the studies' different methodological approaches, they generally reported the deleterious effect of Sed on AS [16, 27].

Contrary to our expectations, MVPA was not an independent predictor of cfPWV. By contrast, an association between meeting international guidelines of PA and lower cfPWV in adults free of established CVD study was demonstrated [4]. However, others have reported results similar to those observed in our study [13]. Future research should seek to clarify the association between MVPA and AS.

MetS entails a cluster of critical metabolic, inflammatory, and hemostatic conditions [2] that affect large arteries at all ages [23–25]. Our data reinforce that description since participants with MetS exhibited worse metabolic, lipid-related, proinflammatory, and AS profiles. However, our data showed that participants with MetS with higher PA and lower Sed have less cfPWV than those with worse PA profiles. As such, PA arguably plays a protective role in humoral and inflammatory secondary effects in AS. Physiological mechanisms linking Sed [3, 21] and MetS [22] to AS suggest impaired glucose metabolism and deterioration in insulin sensitivity. For one, hyperglycemia provokes changes in arterial walls due to protein glycation and the consequent formation of advanced glycation end products in the extracellular matrix, which compromise



▶ **Fig. 1** Carotid-femoral pulse wave velocity according to metabolic syndrome and sedentary behavior and physical activity %"Legend. Carotid-femoral pulse wave velocity means (label inside bars) adjusted for age, according to the presence of metabolic syndrome and to the median of time spent in sedentary behavior **a**, light physical activity **b**, and moderate-to-vigorous physical activity **c**. White and grey bars are participants with and without metabolic syndrome, respectively. Physical activities intensities are divided by the median (median of sedentary behavior = 467 min/day; median of light physical activity = 284 min/day, and median of moderate-to-vigorous physical activity = 30 min/day) * p< 0.05; * * p< 0.001 Page 7, line 157.

arterial distensibility [5, 22]. Sed might furthermore increase pro-inflammatory cytokines [17], which initiate a cascade of inflammatory mediators that target the vascular endothelium, thereby prompting the endothelium dysfunction [17, 21] and the migration and proliferation of smooth muscle cells [17], impairing arterial distensibility [18].

Since individuals with MetS have elevated resting blood pressure, it is important to note that hypertension generates repeated pulsatile stress leading to biomechanical fatigue and related loss of well-ordered arrangement of smooth muscle cells and extracellular matrix [5, 19]. As a consequence, there is a degeneration of elastic fibres, an increased in collagenous material, and often deposition of calcium in arterial walls [5, 19]. Furthermore, the activation of the renin-angiotensin system might contribute to structural alteration of the arterial wall, promoting vascular smooth muscle cell proliferation, low-grade inflammation, increased collagen content, and advanced glycation end product formation, which ultimately augments AS [5, 17, 19].

Our study has some limitations. As an observational, cross-sectional study, it hinders the establishment of causal inferences and suggests associations only.

Moreover, the large percentage of potential participants who declined to participate might have skewed the prevalence of MetS in our study. Although we adjusted all models for multiple variables, the influence of residual confounders cannot be excluded. The small sample size for the age range and the seasonality also influenced the total amount of daily PA, which constitutes a study limitation for future research work to overcome.

We have drawn the following conclusions from our findings. First, in those with MetS, Sed time leads to significantly higher cfPWV. Second, Sed time is also positively associated with cfPWV, independent of age and metabolic risk factors.

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Conflict of Interest

The authors have no conflict of interest to declare.

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